Access DB# 90146

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's full Name: Devesh Khare Examiner #: 77931 Date: 3/27/2003
Art Unit: 1623 Phone Number 605-1199 Serial Number: PCT/US01/05320 / 09/889,287
Mail Box: CM1-8B19 and Bldg/Room Location: CM1-8A13 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be search Include the elected species or structures, key words, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: See Bib Data Sheet

Inventors (please provide full names): See Bib Data Sheet

Point of Contact
Mona Smith
Technical Information Specialist
CM1 6A01
Tel: 308-3278

Earliest priority Filing Date: See Bib Data Sheet

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please carry out a structure search of the [redacted] compounds having the formula set forth in Claims 43-48 enclosed herewith. A search of a method for synthesis of these compounds, Claims 1, 20 and 38 is also requested. A copy of the claims is provided.

The Bib Data Sheet which discloses the inventor names, title of the invention, and the earliest priority filing date is also provided.

Note: Please return the copy of the claims with the search.

Thank you.

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: M. SMITH	NA Sequence (#)	STN
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#) X	Questel/Orbit
Date Searcher Picked Up: 3/29/03	Bibliographic	Dr. Link
Date Completed: 4/24/03	Litigation	Lexis/Nexis
Searcher Prep & Review Time: 75	Fulltext	Sequence Systems
Clerical prep time:	Patent Family	WWW/Internet
Online Time: 60	Other	Other (specify)

PTO-1590 (1-2000)

STIC-STN Search

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> fil hcaplu
FILE 'HCAPLUS' ENTERED AT 15:05:44 ON 25 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 25 Apr 2003 VOL 138 ISS 18
FILE LAST UPDATED: 24 Apr 2003 (20030424/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d stat que
L2 1 SEA FILE=REGISTRY "9H-PURIN-6-AMINE, 2-CHLORO-9-(2-DEOXY-2-FLUO RO-.BETA.-D-ARABINOFURANOSYL)-"/CN
L3 SEL L2 1- CHEM : 3 TERMS
L4 43 SEA FILE=HCAPLUS L3
L5 19 SEA FILE=HCAPLUS L4 AND (SYNTHES? OR PREP? OR MANUF?)

=> d ibib abs hitrn 15 1-9

L5 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:117837 HCAPLUS
DOCUMENT NUMBER: 138:122813
TITLE: Process for **preparing** purine arabinofuranosyl nucleosides via stereoselective glycosylation of nucleobase salts
INVENTOR(S): Bauta, William E.; Schulmeier, Brian E.; Cantrell, William R., Jr.; Lovett, Dennis; Puente, Jose
PATENT ASSIGNEE(S): Ilex Oncology Inc., USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011877	A2	20030213	WO 2002-US24392	20020801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

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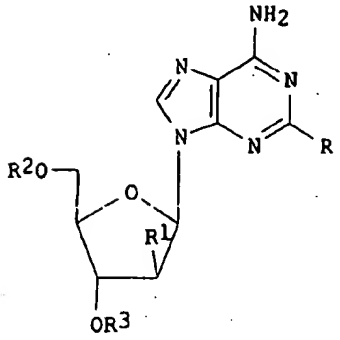
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-309590P P 20010802
OTHER SOURCE(S): MARPAT 138:122813
GI



I

AB The present invention provides for the **prepn**. .beta.-adenine nucleosides I, wherein R is halogen, NH2; R1-R3 are independently H, hydroxy protecting group; by coupling an adenine deriv. contg. an unprotected exocyclic amino group at the C-6 position and a blocked arabinofuranosyl deriv., in the presence of a base and solvent. The present invention also provides for the stereoselective **prepn**. of 2-deoxy-.beta.-D-adenine nucleosides wherein a blocked 2-deoxy-.beta.-D-arabinofuranosyl halide is coupled with the salt of an adenine deriv. The forgoing aspects of the present invention are utilized in the **prepn**. of a **clofarabine** I (R = Cl, R1-R3 = H) wherein the ratio of .beta. to .alpha.-anomer is at least 99:1.

IT **123318-82-1P**
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(conformation; process for prepg. purine arabinofuranosyl nucleosides via stereoselective glycosylation of nucleobase salts)

L5 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:657258 HCAPLUS
DOCUMENT NUMBER: 136:6249
TITLE: **Synthesis** and biological activity of 4'-C-hydroxymethyl-2'-fluoro-D-arabinofuranosylpurine nucleosides
AUTHOR(S): Shortnacy-Fowler, Anita T.; Tiwari, Kamal N.; Montgomery, John A.; Secrist, John A., III
CORPORATE SOURCE: Southern Research Institute, Birmingham, AL, 35255-5305, USA
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2001), 20(8), 1583-1598

Searched by M. Smith

CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 4'-C-hydroxymethyl-2'-fluoro-D-arabinofuranosylpurine nucleosides was prepd. and evaluated for cytotoxicity. The details of a convenient synthesis of the carbohydrate precursor 4-C-hydroxymethyl-3,5-di-O-benzoyl-2-fluoro-.alpha.-D-arabinofuranosyl bromide are presented. Proof of the structure and configuration at all chiral centers of the sugars and the nucleosides were obtained by proton NMR. All five target nucleosides were evaluated for cytotoxicity in human tumor cell lines. The 4'-C-hydroxymethyl clofarabine analog showed slight cytotoxicity in CCRF-CEM leukemia cells.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:617838 HCAPLUS
DOCUMENT NUMBER: 135:180927
TITLE: Improved methods for synthesizing 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-9h-purin-6-amine
INVENTOR(S): Montgomery, John A.; Fowler, Anita T.; Secrist, John A., III
PATENT ASSIGNEE(S): Southern Research Institute, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060383	A1	20010823	WO 2001-US5320	20010216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1261350	A1	20021204	EP 2001-910961	20010216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003023078	A1	20030130	US 2001-889287	20010716

PRIORITY APPLN. INFO.: US 2000-183422P P 20000218
WO 2001-US5320 W 20010216

OTHER SOURCE(S): CASREACT 135:180927
AB This invention relates to improved methods for synthesizing 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-9h-purin-6-amine, a chemotherapeutic agent that is useful in the treatment of various malignancies. Thus, 2,6-dichloropurine in MeCN is treated with NaH and reacted with 2-deoxy-2-fluoro-3,5-di-O-benzoyl-.alpha.-D-arabinofuranosyl bromide; this product was suspended in MeOH and treated with NaOMe to give 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-6-methoxy-9h-purine in 60% yield; this was reacted with ammonia to provide

2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-9H-purin-6-amine in 78% yield. The present method results in increased yields over previously reported methods.

IT **123318-82-1P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(improved methods for **synthesizing** 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-9h-purin-6-amine)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:64771 HCAPLUS
DOCUMENT NUMBER: 134:296041
TITLE: Oligonucleotides containing 9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-adenine and -guanine: **synthesis**, hybridization and antisense properties
AUTHOR(S): Tennila, Tuula; Azhayeva, Elena; Vepsalainen, Jouko; Laatikainen, Reino; Azhayev, Alex; Mikhailopulo, Igor A.
CORPORATE SOURCE: Departments of Pharmaceutical Chemistry, University of Kuopio, Kuopio, FIN-70211, Finland
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2000), 19(10-12), 1861-1884
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:296041

AB **Synthesis** of 9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-adenine (I) and -guanine (II) was accomplished via the condensation of 2,6-dichloropurine with 2-deoxy-2-fluoro-1,3,5-tri-O-benzoyl-.alpha.-D-arabinofuranose as a key chem. step. Condensation of silylated N6-benzoyladenine with 2 gave, after deblocking and chromatog. sepn., I (14%), it's .alpha.-anomer (14%) and N7-.alpha.-isomer (25%). The PSEUROT anal. of N9-.beta.-D-arabinosides I and II manifested slight preference for the S rotamer (64%) for the former, and an equal population of the N and S rotamers for the latter. The arabinosides I and II were used for the **prepn**. of the resp. phosphoramidite building blocks for automated oligonucleotide **synthesis**. Four 15-mer oligonucleotides (ONs) complementary to the initiation codon region of firefly luciferase mRNA were **prepd**.: unmodified 2'-deoxy-ON (AS1) and contg. (i) I instead of the only A (AS2), (ii) II vs. 3-G from the 5'-terminus (AS3), and (iii) both arabinosides at the same positions (AS4). All these ONs display practically the same (i) affinity to both complementary DNA and RNA, and (ii) ability to inhibit a luciferase gene expression in a cell-free transcription-translation system.

IT **123318-82-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(oligonucleotides contg. deoxyfluorobarabinofuranosyladenine and guanine **synthesis** hybridization and antisense properties)

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:703903 HCAPLUS
DOCUMENT NUMBER: 132:231574

TITLE: Treatment of normal and malignant cells with nucleoside analogues and etoposide enhances deoxycytidine kinase activity
AUTHOR(S): Spasokoukotskaja, T.; Sasvari-Szekely, M.; Keszler, G.; Albertioni, F.; Eriksson, S.; Staub, M.
CORPORATE SOURCE: Department of Medical Chemistry, Molecular Biology and Pathobiochemistry, Semmelweis University of Medicine, Budapest, H-1444, Hung.
SOURCE: European Journal of Cancer (1999), 35(13), 1862-1867
CODEN: EJCAEL; ISSN: 0959-8049
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Deoxycytidine kinase (dCK), one of the rate-limiting enzymes in the intracellular metab. of many antileukemic drugs, has been shown to be stimulated after treatment of human tonsillar lymphocytes by 2-chloro-2'-deoxyadenosine (cladribine, CdA). The present work presents a comparative study of different normal and malignant cells in respect to the activation of dCK by CdA. G-phase lymphocytes showed a higher sensitivity for dCK stimulation than S-phase cells. Normal and leukemic peripheral blood mononuclear cells, as well as the promyelocytic cell line HL60, responded to CdA treatment by a 2-5-fold increase in activity of dCK. However, no significant stimulation was detected either in CCRF-CEM T-lymphoblastoid cells or in K562 myeloid cells. Thymidine kinase activity was not stimulated in any cases. Treatment of these cells with several other analogs beside CdA, such as 2-chloro-2'-arabino-fluoro-2'-deoxyadenosine, 2-fluoro-1-.beta.-D-arabinosyladenine (Fludarabine) and 1-.beta.-D-arabinosylcytosine (cytarabine, araC) gave results similar to those of CdA treatment. Enhancement of dCK activity could also be achieved with the topoisomerase II inhibitor etoposide. In contrast, 2-chlororiboadenosine had no effect on the dCK at concns. of .ltoreq.10 .mu.M, while deoxycytidine and 5-azadeoxycytidine caused slight inhibition. These results indicate that treatment of cells with several inhibitors of DNA synthesis potentiates the dCK activity. The drugs widely differ in their stimulatory effect on dCK, and there are also 'responsive' and 'nonresponsive' cells with respect to dCK activation. Thus, enhancement of the dCK activity by specific drugs in 'responsive' cells might give a rationale for combination chemotherapy.

IT **123318-82-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(nucleoside analogs and etoposide effect on deoxycytidine kinase activity in normal and malignant cells)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:191826 HCAPLUS
DOCUMENT NUMBER: 130:217817
TITLE: Antitumor activity of **2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl) adenine**, a novel deoxyadenosine analog, against human colon tumor xenografts by oral administration
AUTHOR(S): Takahashi, Takeshi; Kanazawa, Junji; Akinaga, Shiro; Tamaoki, Tatsuya; Okabe, Masami
CORPORATE SOURCE: Cancer Chemotherapy, Pharmaceutical Research Inst., Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411, Japan

Searched by M. Smith

SOURCE: Cancer Chemotherapy and Pharmacology (1999), 43(3), 233-240
CODEN: CCPHD2; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **2-Chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl) adenine** (Cl-F-araA) is a novel deoxyadenosine analog, which inhibits DNA **synthesis** by inhibiting DNA polymerase .alpha. and ribonucleotide reductase. Cl-F-araA shows potent antiproliferative activity against several leukemic cell lines including those of human origin and is also effective against murine solid tumors, in particular being curative against colon tumors. It was investigated whether Cl-F-araA is effective against human colon tumors, in particular by oral administration, since it has improved stability compared with other deoxyadenosine analogs. Antiproliferative activity in vitro was detd. from cell counts. S.c. inoculated xenograft models and a liver micrometastases model were used for assessment of antitumor activity in vivo. Cl-F-araA showed potent antiproliferative activity against 4 human colon tumor cell lines (HCT116, HT-29, DLD-1, WiDr), with a 50% growth-inhibitory concn. (IC50) of 0.26 .mu.M with a 72-h exposure. This activity was greater than those of fludarabine desphosphate and cladribine, other deoxyadenosine analogs, which showed IC50 values of 19 and 0.35 .mu.M, resp. Cl-F-araA showed potent antitumor activity against 4 human colon tumor xenograft models (HT-29, WiDr, Co-3, COLO-320DM) in a 5-day daily administration schedule, which was shown to be the most effective of 3 administration regimens tested (single, twice-weekly, 5-day daily). In particular, oral administration showed superior activity, with a regressive or cytostatic growth curve, compared with i.v. administration. In addn., Cl-F-araA was effective at only 1/16 of the max. dose tested in a 10-day daily administration schedule. Therapeutic efficiency seemed to increase in proportion to the frequency of administration. Cl-F-araA also decreased liver micrometastases created by intrasplenic injection of human colon tumor cells, leading to complete suppression at the max. dose tested. These results suggest that Cl-F-araA might be clin. effective against human colon cancers using a daily oral administration schedule.

IT **123318-82-1, 2-Chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl) adenine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of **2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl) adenine** against human colon tumor xenografts by oral administration)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:171085 HCAPLUS
DOCUMENT NUMBER: 130:346991
TITLE: Comparison of the mechanism of cytotoxicity of **2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl) adenine**, 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-

ribofuranosyl)adenine, and 2-chloro-9-(2-deoxy-2,2-difluoro-.beta.-D-ribofuranosyl)adenine in CEM cells

AUTHOR(S): Parker, William B.; Shaddix, Sue C.; Rose, Lucy M.; Shewach, Donna S.; Hertel, Larry W.; Secrist, John A., III; Montgomery, John A.; Bennett, L. Lee, Jr.

CORPORATE SOURCE: Southern Research Institute, Birmingham, AL, USA

SOURCE: Molecular Pharmacology (1999), 55(3), 515-520
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In an effort to understand biochem. features that are important to the selective antitumor activity of **2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)adenine** [Cl-F(.uparw.)-dAdo], we evaluated the biochem. pharmacol. of three structurally similar compds. that have quite different antitumor activities. Cl-F(.uparw.)-dAdo was 50-fold more potent as an inhibitor of CEM cell growth than were either 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-ribofuranosyl)adenine [Cl-F(.dwnarw.)-dAdo] or 2-chloro-9-(2-deoxy-2,2-difluoro-.beta.-D-ribofuranosyl)adenine [Cl-diF(.uparw..dwnarw.)-dAdo]. The compds. were similar as substrates of deoxycytidine kinase. Similar amts. of their resp. triphosphates accumulated in CEM cells, and the rate of disappearance of these metabolites was also similar. Cl-F(.uparw.)-dAdo was 10- to 30-fold more potent in its ability to inhibit the incorporation of cytidine into deoxycytidine nucleotides than either Cl-F(.dwnarw.)-dAdo or Cl-diF(.uparw..dwnarw.)-dAdo, resp., which indicated that ribonucleotide reductase was differentially inhibited by these three compds. Thus, the differences in the cytotoxicity of these agents toward CEM cells were not related to quant. differences in the phosphorylation of these agents to active forms but can mostly be accounted for by differences in the inhibition of ribonucleotide reductase activity. Furthermore, the inhibition of RNA and protein synthesis by Cl-F(.dwnarw.)-dAdo and Cl-diF(.uparw..dwnarw.)-dAdo at concns. similar to those required for the inhibition of DNA synthesis can help explain the poor antitumor selectivity of these two agents because all cells require RNA and protein synthesis.

IT **123318-82-1, 2-Chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)adenine**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(mechanism of cytotoxicity of chlorodeoxyfluoroarabinofuranosyl adenine in CEM cells)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:132780 HCAPLUS

DOCUMENT NUMBER: 126:139875

TITLE: Nucleotide analogs, their preparation, and pharmaceutical compositions containing them for topical treatment of proliferative disease of the skin

INVENTOR(S): Hostetler, Karl Y.

PATENT ASSIGNEE(S): Hostetler, Karl Y., USA

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640166	A1	19961219	WO 1996-US10084	19960606
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5654286	A	19970805	US 1995-485025	19950607
AU 9662737	A1	19961230	AU 1996-62737	19960606
EP 831855	A1	19980401	EP 1996-921531	19960606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002515018	T2	20020521	JP 1997-502193	19960606

PRIORITY APPLN. INFO.: US 1995-485025 A 19950607
US 1993-60258 A2 19930512
WO 1996-US10084 W 19960606

OTHER SOURCE(S): MARPAT 126:139875

AB Pharmaceutical compns. are disclosed which contain mono-, di-, and triphosphate esters of antiproliferative nucleoside analogs, DNA chain-terminating dideoxynucleoside analogs and other nucleoside analogs for the topical treatment of hyperproliferative diseases of the skin (psoriasis, atopic dermatitis, basal cell carcinoma, etc.). The useful phosphate esters of the nucleoside analogs include phosphoramidates and phosphothioates, as well as polyphosphates having C and S bridging atoms.

IT **123318-82-1DP**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide analogs, **prepn.**, and pharmaceutical compns. for topical treatment of proliferative skin diseases)

L5 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:555956 HCAPLUS
DOCUMENT NUMBER: 125:237782
TITLE: Metabolism and actions of 2-chloro-2'-fluoroarabinosyladenine (chlorofluoroarabinosyladenine, ribonucleotide reductase, DNA **synthesis**, apoptosis)
AUTHOR(S): Xie, Kevin Chunxi
CORPORATE SOURCE: Health Science Center, Univ. of Texas, Houston, TX, USA
SOURCE: (1996) 227 pp. Avail.: From degree-granting institution
From: Diss. Abstr. Int., B 1996, 57(4), 2507
DOCUMENT TYPE: Dissertation
LANGUAGE: English

AB Unavailable

IT **123318-82-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metab. and action of chlorofluoroarabinosyladenine)

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L5 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:394751 HCAPLUS
DOCUMENT NUMBER: 125:104437
TITLE: Deoxynucleotide pool depletion and sustained inhibition of ribonucleotide reductase and DNA synthesis after treatment of human lymphoblastoid cells with 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)adenine
AUTHOR(S): Xie, Kevin Chunxi; Plunkett, William
CORPORATE SOURCE: Dep. Clin. Invest., Univ. Texas M. D. Anderson Cancer Cent., Houston, TX, 77030, USA
SOURCE: Cancer Research (1996), 56(13), 3030-3037
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The action of the new adenine nucleoside analog 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)adenosine (Cl-F-ara-A) on DNA synthesis was evaluated both in whole cells and in vitro assay systems with purified DNA polymerases. [3H]Thymidine incorporation into DNA in human lymphoblastoid CEM cells was inhibited by Cl-F-ara-A in a concn.-dependent manner that was not reversed 72 h after removal of Cl-F-ara-A from the medium. Deoxynucleotide pools were depressed after incubation of Cl-F-ara-A for 3 h and only partially recovered following washing the cells into drug-free medium. The most pronounced decrease occurred in the dCTP pool, quant. followed by the dATP, dCTP, and dTTP pools. This was in concordance with the results of in situ assays of ribonucleotide reductase, which demonstrated profound inhibition of CDP redn. in cells incubated with Cl-F-ara-A; redn. of ADP, GDP, and UDP were affected to lesser extents. Reductase activity was inversely correlated with the cellular Cl-F-ara-ATP level, and inhibition of the enzyme was satd. when cellular Cl-F-ara-ATP reached 25 .mu.M. In vitro DAN primer extension assays indicated that Cl-F-ara-ATP competed with dATP for incorporation into A sites of the extending DNA strand catalyzed by both human DNA polymerases .alpha. and .epsilon.. The incorporation of Cl-F-ara-AMP into DNA inhibited DNA strand elongation; the most pronounced effect was obsd. at Cl-F-ara-ATP:dATP values >1. The sustained inhibition of ribonucleotide reductase and the consequent depletion of deoxynucleotide triphosphate pools results in a cellular concn. ratio of dATP to Cl-F-ara-ATP, which favors analog incorporation into DNA, an action that has been strongly correlated with loss of viability. The results are discussed in relation to the antitumor mechanism of action of Cl-F-ara-A.

IT 123318-82-1, 2-Chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)adenine
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(deoxynucleotide pool depletion and sustained inhibition of ribonucleotide reductase and DNA synthesis after treatment of human lymphoblastoid cells with chloro(deoxyfluoroarabinofuranosyl)adenine in relation to antitumor activity)

L5 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:448973 HCAPLUS
DOCUMENT NUMBER: 122:260176
TITLE: **Preparative** high-performance liquid chromatographic separation of fluorodeoxy sugars
AUTHOR(S): Evangelisto, Mary F.; Adams, Richard E.; Murray, William V.; Caldwell, Gary W.
CORPORATE SOURCE: The R.W. Johnson Pharmaceutical Research Institute, 1000 Route 202, Raritan, NJ, 08869-0602, USA
SOURCE: Journal of Chromatography, A (1995), 695(1), 128-31
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Normal- and reversed-phase **preparative** chromatog. methods were developed to isolate gram quantities of anal. pure 6-amino-2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-9H-purine (arafluoro-2-CdA; RWJ 29727) and its .alpha.-anomer (RWJ 48667). The complex reaction mixt. (.apprx.171 g), from a Parr Bomb **synthesis**, was **prepurified** by normal-phase chromatog. to yield .apprx.40 g. Twelve reversed-phase **preparative** isolations were run on a custom-packed YMC column to yield .apprx.12 g of arafluoro-2-CdA (99.7%) and .apprx.3 g of the .alpha.-anomer (99.2%).
IT **123318-82-1P**
RL: PUR (Purification or recovery); PREP (Preparation)
(**preparative** HPLC sepn. of fluorodeoxy sugars)

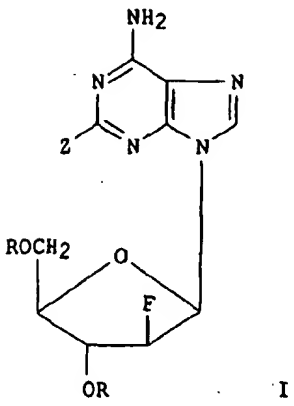
L5 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:383007 HCAPLUS
DOCUMENT NUMBER: 122:291456
TITLE: Antineoplastic 2'-fluoro-2-haloarabinoadenosines and their pharmaceutical compositions
INVENTOR(S): Montgomery, John A.; Secrist, John A., III
PATENT ASSIGNEE(S): Southern Research Institute, USA
SOURCE: U.S., 8 pp. Cont.-in-part of U.S. 5,034,518.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5384310	A	19950124	US 1991-693646	19910510
US 5034518	A	19910723	US 1989-355358	19890523
AT 147751	E	19970215	AT 1990-909080	19900523
ES 2098266	T3	19970501	ES 1990-909080	19900523
CA 2102782	AA	19921111	CA 1992-2102782	19920507
WO 9220347	A1	19921126	WO 1992-US3889	19920507
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
EP 595826	A1	19940511	EP 1992-912163	19920507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06507644	T2	19940901	JP 1992-500121	19920507
US 5661136	A	19970826	US 1994-320879	19940921

PRIORITY APPLN. INFO.: US 1989-355358 A2 19890523
US 1991-693646 A 19910510
WO 1992-US3889 W 19920507

Searched by M. Smith

OTHER SOURCE(S): MARPAT 122:291456
GI



I

AB The present invention is directed to certain 2'-fluoro, 2-substituted purine nucleosides I (wherein R, each which may be the same or different, is hydrogen or a protecting group; wherein Z is a halogen of the group F, Cl, and Br; and pharmaceutically acceptable salts thereof, said compn. being in combination with a pharmaceutically acceptable carrier for oral, topical, or parenteral administration) which are toxic to cancerous cell lines. Cytotoxicity [as IC50(.mu.M)] of 2-haloadenine nucleosides against cancer cells (3 human cell lines and a murine leukemia line): from 0.003 to 4. Studies with the P388 leukemia cell line in mice indicate that the most effective compd. of the present invention is 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-9H-purin-6-amine: at a dose of 20 mg/kg, median % ILS (increase in life span) was 220%.

IT **123318-82-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antineoplastic 2'-fluoro-2-haloarabinoadenosines)

L5 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:442767 HCAPLUS
DOCUMENT NUMBER: 121:42767
TITLE: Pharmaceutical compositions containing 2-halo-2'-deoxyadenosines in the treatment of rheumatoid arthritis
INVENTOR(S): Carson, Dennis A.; Carrera, Carlos J.
PATENT ASSIGNEE(S): Scripps Research Institute, USA
SOURCE: U.S., 25 pp. Cont.-in-part of U.S. 5,106,837.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5310732	A	19940510	US 1992-838546	19920219
US 5106837	A	19920421	US 1990-460351	19900103

Searched by M. Smith

WO 9316706		A1	19930902	WO 1993-US1467	19930218
W:	AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9337249		A1	19930913	AU 1993-37249	19930218
AU 682818		B2	19971023		
CH 684310		A	19940831	CH 1993-3143	19930218
EP 626853		A1	19941207	EP 1993-906071	19930218
EP 626853		B1	20000426		
R:	AT, BE, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
HU 68030		A2	19950529	HU 1994-2392	19930218
HU 218656		B	20001028		
JP 07507540		T2	19950824	JP 1993-514960	19930218
BR 9305907		A	19971021	BR 1993-5907	19930218
RU 2130308		C1	19990520	RU 1994-38043	19930218
AT 192045		E	20000515	AT 1993-906071	19930218
US 5541164		A	19960730	US 1994-233056	19940426
US 5506213		A	19960409	US 1994-246328	19940519
CA 2191230		AA	19951207	CA 1994-2191230	19940526
CA 2191230		C	20010227		
WO 9532718		A1	19951207	WO 1994-US5971	19940526
W:	AU, CA, JP, US				
RW:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9474707		A1	19951221	AU 1994-74707	19940526
JP 10505323		T2	19980526	JP 1994-500782	19940526
NO 9402765		A	19940913	NO 1994-2765	19940725
US 5506214		A	19960409	US 1994-256931	19940727
FI 9403805		A	19941019	FI 1994-3805	19940818
AU 9918593		A1	19990506	AU 1999-18593	19990304
AU 735319		B2	20010705		

PRIORITY APPLN. INFO.:	US 1986-825215	B2	19860203
	US 1988-169618	B2	19880316
	US 1989-323350	B2	19890314
	US 1990-460351	A2	19900103
	US 1992-838546	A1	19920219
	WO 1993-US1467	A	19930218
	US 1994-233056	A3	19940426
	AU 1994-74707	A3	19940526
	WO 1994-US5971	A	19940526

AB The title compns. contg. novel adenine derivs. are prepd. to treat monocyte-mediated disorders such as rheumatoid arthritis and multiple sclerosis. Exposure of cultured human monocytes to 20 nm 2-chlorodeoxyadenosine over a 5 days culture period at 37.degree. killed 50% of monocytes. Thus, 2,6-dichloro-9,1'(3'-O-acetyl-5'-O-benzoyl-2'-deoxy-2'-fluoro-beta-D-arabinofuranosyl)-9-purine (prepn. given) was reacted with methanolic ammonia to produce 2-chloro-9-beta-2'-deoxy-21-fluoro-D-arabinofuranosyladenine (I). A tablet contained I 1, starch 40, modified starch 10, Mg stearate 1-5 mg, and CaHPO4 q.s.

IT **123318-82-1P**
RL: PREP (Preparation)
(prepn. of, pharmaceutical compns. contg., for treatment of rheumatoid arthritis)

L5 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:192189 HCAPLUS
DOCUMENT NUMBER: 118:192189
TITLE: 2'-fluoro-2-substituted adeninylarabinosides as anticancer agents

INVENTOR(S): Montgomery, John A.; Secrist, John A.
PATENT ASSIGNEE(S): Southern Research Institute, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9220347	A1	19921126	WO 1992-US3889	19920507
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5384310	A	19950124	US 1991-693646	19910510
EP 595826	A1	19940511	EP 1992-912163	19920507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06507644	T2	19940901	JP 1992-500121	19920507

PRIORITY APPLN. INFO.: US 1991-693646 A 19910510
US 1989-355358 A2 19890523
WO 1992-US3889 W 19920507
OTHER SOURCE(S): MARPAT 118:192189
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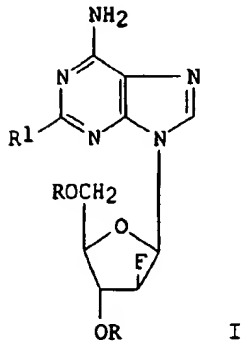


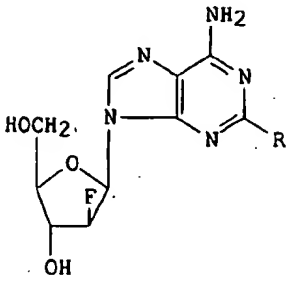
I

AB Title compds. I (R = H, protective group; R1 = F, Cl, Br) were prepd. Thus, I (R = H, R1 = Cl) was obtained in 42.3% yield by treating the protected 2,6-dichloropurine analog with NH3 in EtOH. I (R = H, R1 = Cl) had a cytotoxic ED50 against H.Ep-2 cells of 0.012 .mu.M, cf. 0.03 for the 2'-deoxy analog.
IT 123318-82-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cytotoxicity of)

L5 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:152261 HCAPLUS
DOCUMENT NUMBER: 116:152261
TITLE: Synthesis and biological activity of 2'-fluoro-2-halo derivatives of 9-.beta.-D-arabinofuranosyladenine
AUTHOR(S): Montgomery, John A.; Shortnacy-Fowler, Anita T.; Clayton, Sarah D.; Riordan, James M.; Secrist, John A., III

Searched by M. Smith

CORPORATE SOURCE: South. Res. Inst., Birmingham, AL, 35255-5305, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(2), 397-401
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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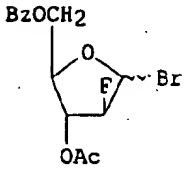

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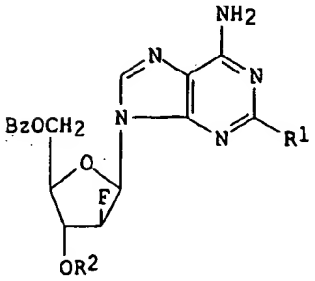

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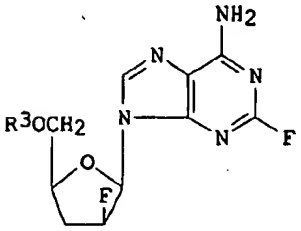

IV

AB The synthesis of 2-halo-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)adenines I (R = Br, Cl) by coupling the 2,6-dihalopurine with 2-deoxy-2-fluoro-D-arabinofuranosyl bromide II followed by replacement of the 6-halogen with concomitant removal of the acyl blocking groups is described. 2-Fluoroadenine deriv. I (R = F) had to be prepd. by the diazotization-fluorination of 2-aminoadenine nucleoside III (R1 = NH2, R2 = Ac). All three nucleosides provided good increases in life span of mice inoculated with P388 leukemia. The best results were obtained when the compds. were administered q3h.times.8 on days 1, 5, and 9 after implantation of the leukemia cells. The 2',3'-dideoxynucleoside IV (R3 = H), prepd. by deacetylation of III (R1 = F, R2 = Ac) and deoxygenation of the resultant III (R1 = F, R2 = H) followed by removal of the benzoyl group of IV (R3 = Bz), was slightly active against HIV in cell culture.

IT **123318-82-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antitumor activity of)

L5 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:421747 HCAPLUS
DOCUMENT NUMBER: 115:21747

TITLE: Effects of 2-chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)adenine on K562 cellular metabolism and the inhibition of human ribonucleotide reductase and DNA polymerases by its 5'-triphosphate

AUTHOR(S): Parker, William B.; Shaddix, Sue C.; Chang, Chi Hsiung; White, E. Lucile; Rose, Lucy M.; Brockman, R. Wallace; Shortnacy, Anita T.; Montgomery, John A.; Secrist, John A., III; Bennett, L. Lee, Jr.

CORPORATE SOURCE: Kettering-Meyer Lab., South. Res. Inst., Birmingham, AL, 35205, USA

SOURCE: Cancer Research (1991), 51(9), 2386-94
CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2-Chloro-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-adenine (Cl-F-ara-A) has activity against the P388 tumor in mice on several different schedules. Biochem. studies with a chronic myelogenous leukemia cell line (K562) grown in cell culture have been done in order to better understand its mechanism of action. Cl-F-ara-A was a potent inhibitor of K562 cell growth. Only 5 nM inhibited K562 cell growth by 50% after 72 h of continuous incubation. The 5'-triphosphate of Cl-F-ara-A was detected by strong anion exchange chromatog. of the acid-sol. ext. of K562 cells incubated with Cl-F-ara-A. Competition studies with natural nucleosides suggested that deoxycytidine kinase was the enzyme responsible for the metab. to the monophosphate. Incubation of K562 cells for 4 h with 50 nM Cl-F-ara-A inhibited the incorporation of [3H]thymidine into the DNA by 50%. Incubation with 0.1, 1, or 10 .mu.M Cl-F-ara-A for 4 h depressed dATP, dCTP, and dGTP pools but did not affect TTP pools. Similar inhibition of deoxyribonucleoside triphosphate pools was seen after incubation with 2-chloro-2'-deoxyadenosine. Both Cl-F-ara-ATP and Cl-dATP potently inhibited the redn. of ADP to dADP in crude exts. of K562 cells (concn. producing 50% inhibition, 65 nM). The effect of Cl-F-ara-ATP on human DNA polymerases .alpha., .beta., and .gamma. isolated from K562 cells grown in culture was detd. and compared with those of Cl-dATP and 9-.beta.-D-arabinofuranosyl-2-fluoroadenine triphosphate (F-ara-ATP). Cl-F-ara-ATP was a potent inhibitor of DNA polymerase .alpha.. Inhibition of DNA polymerase .alpha. was competitive with respect to dATP (Ki of 1 .mu.M). The three analog triphosphates were incorporated into the DNA by DNA polymerase .alpha. as efficiently as dATP. The incorporation of Cl-F-ara-AMP inhibited the further elongation of the DNA chain, similarly to that seen after the incorporation of F-ara-AMP. Extension of the DNA chain after the incorporation of Cl-dAMP was not inhibited as much as it was with either Cl-F-ara-AMP or F-ara-AMP. Cl-F-ara-ATP was not a potent inhibitor of DNA polymerase .beta., DNA polymerase .gamma., or DNA primase. These results indicate that the inhibition of DNA synthesis by Cl-F-ara-A was due to the inhibition of ribonucleotide reductase activity and inhibition of chain elongation by DNA polymerase .alpha. and that, with respect to inhibition of these enzymes, Cl-F-ara-A incorporates the best properties of F-ara-A and 2-chloro-2'-deoxyadenosine into one compd.

IT 123318-82-1
RL: PRP (Properties)
(antitumor effect of, inhibition of human ribonucleotide reductase and DNA polymerase by its triphosphate in)

L5 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1991:409260 HCAPLUS
DOCUMENT NUMBER: 115:9260
TITLE: Preparation of 2-halo-9-(2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)adenine nucleosides as anticancer agents
INVENTOR(S): Montgomery, John A.; Secrist, John A., III
PATENT ASSIGNEE(S): Southern Research Institute, USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9014352	A1	19901129	WO 1990-US2927	19900523
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 5034518	A	19910723	US 1989-355358	19890523
AU 9058315	A1	19901218	AU 1990-58315	19900523
EP 473708	A1	19920311	EP 1990-909080	19900523
EP 473708	B1	19970115		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05502014	T2	19930415	JP 1990-508789	19900523
JP 3160288	B2	20010425		
AT 147751	E	19970215	AT 1990-909080	19900523
ES 2098266	T3	19970501	ES 1990-909080	19900523

PRIORITY APPLN. INFO.: US 1989-355358 A 19890523
WO 1990-US2927 A 19900523
OTHER SOURCE(S): MARPAT 115:9260
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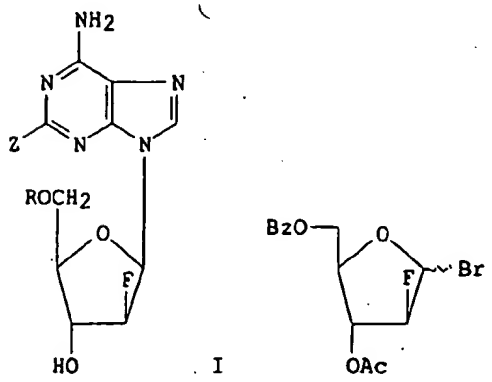

AB The title compds. (I; Z = F, Cl, Br; R = H, acyl), useful in treatment of cancer, e.g., chronic lymphocytic leukemia, were prepd. Glycosylation of 2,6-dibromopurine with .beta.-D-arabinofuranosyl bromide II gave arabinofuranosyldibromopurine deriv. which was treated by ethanolic NH3 to give, after hydrolysis (LiOH), I (Z = Br, R = H), which had an IC50 of 0.60 .mu.M against L1210 cells.
IT 123318-82-1P

Searched by M. Smith

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as anticancer agent)

L5 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:491460 HCAPLUS
DOCUMENT NUMBER: 113:91460
TITLE: Substituted adenine derivatives useful as therapeutic agents
INVENTOR(S): Carson, Dennis A.; Carrera, Carlos J.
PATENT ASSIGNEE(S): Scripps Clinic and Research Foundation, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8908658	A1	19890921	WO 1989-US1088	19890316
W: AU, DK, FI, JP, KR, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8934105	A1	19891005	AU 1989-34105	19890316
AU 626296	B2	19920730		
EP 364559	A1	19900425	EP 1989-904431	19890316
EP 364559	B1	19950920		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03501258	T2	19910322	JP 1989-504299	19890316
JP 3090456	B2	20000918		
AT 128141	E	19951015	AT 1989-904431	19890316
CA 1339964	A1	19980721	CA 1989-593979	19890316
DK 8905721	A	19891115	DK 1989-5721	19891115
DK 170629	B1	19951120		
NO 8904558	A	19891115	NO 1989-4558	19891115
CA 2191230	AA	19951207	CA 1994-2191230	19940526
CA 2191230	C	20010227		
AU 9474707	A1	19951221	AU 1994-74707	19940526
JP 10505323	T2	19980526	JP 1994-500782	19940526
AU 9918593	A1	19990506	AU 1999-18593	19990304
AU 735319	B2	20010705		

PRIORITY APPLN. INFO.:
US 1988-169618 A 19880316
US 1989-323350 A 19890314
WO 1989-US1088 A 19890316
AU 1994-74707 A3 19940526
WO 1994-US5971 A 19940526

OTHER SOURCE(S): MARPAT 113:91460
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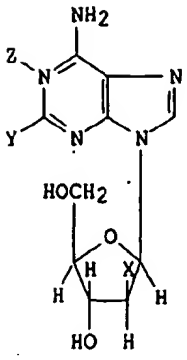

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AB Substituted adenine derivs. I (e.g. Z = O or absent; Y = H or a substituent contg. 1-20 atoms that is free from net ionic charge at physiol. pH values; X = H or F; when Z is absent, X = F; Y is H only when Z is present and X = F) are effective in treating autoimmune diseases and monocyte-mediated disorders. For treating monocyte-mediated diseases, an antimicrobial agent in addn. to I may be administered. EDs of I for treating monocyte-mediated disease, autoimmune disease (i.e. rheumatoid arthritis), and AIDS are claimed. No therapeutic tests are given. In vitro as well as in vivo cytotoxicity of 2-chlorodeoxyadenosine is described. Thus, 2-chloro-9,1'-.beta.-2'-deoxy-2'-fluoro-D-arabinofuranosyl adenine (II) was **prepd.** starting from 1,3'-di-O-acetyl-5'-O-benzoyl-2'-deoxy-2'-fluoro-.beta.-D-arabinose via 3'-O-acetyl-5'-O-benzoyl-2'-deoxy-2-fluoro-D-arabinofuranosyl bromide and 2,6'-dichloro-9,1'-(3'-O-acetyl-5-O-benzoyl-2'-deoxy-2'-fluoro-.beta.-D-arabinofuranosyl)-9-purine. Tablets were **prepd.** contg. II 1, starch 40, modified starch 10, Mg stearate 1-5 mg and CaHPO4 q.s.

IT **123318-82-1**
RL: BIOL (Biological study)
(pharmaceuticals contg., for treating autoimmune and monocyte-mediated diseases)

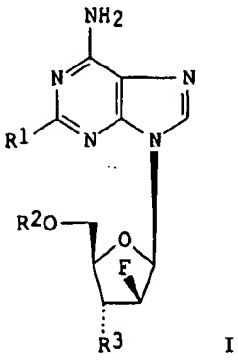
IT **123318-82-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(**prepn.** of, for treating autoimmune or monocyte-mediated diseasesmonocyte-mediated disease)

L5 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:595337 HCAPLUS
DOCUMENT NUMBER: 111:195337
TITLE: **Preparation** of purine derivatives as antivirals and pharmaceutical compositions containing them
INVENTOR(S): Lambert, Robert Wilson; Martin, Joseph Amstrong
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 314011	A2	19890503	EP 1988-117572	19881021
EP 314011	A3	19900411		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8807903	A	19890628	ZA 1988-7903	19881021
AU 8824160	A1	19890504	AU 1988-24160	19881024
CS 270249	B2	19900613	CS 1988-7057	19881025
HU 48270	A2	19890529	HU 1988-5588	19881026
HU 199502	B	19900228		
FI 8804954	A	19890501	FI 1988-4954	19881027
DK 8806037	A	19890501	DK 1988-6037	19881028
NO 8804830	A	19890502	NO 1988-4830	19881028
NO 168037	B	19910930		
NO 168037	C	19920108		
JP 01149797	A2	19890612	JP 1988-271119	19881028
CN 1038102	A	19891220	CN 1988-107516	19881028
PRIORITY APPLN. INFO.:			GB 1987-25466	19871030
			GB 1988-16612	19880713

OTHER SOURCE(S): MARPAT 111:195337
GI



I

AB The title compds. [I; R1 = Cl, N3, NH2; R2 = H, (substituted) trityl; R3 = H, OH, PhOC(S)O] and the amido derivs. and Schiff bases of I [R1 = Cl, N3, NH2; R2 = R3 = H], useful as antiviral agents for humans and animals, esp. useful for the prevention and treatment of infections caused by HIV (no data), are prepd. I [R1 = Cl, R2 = trityl, R3 = H] in CHCl3 was treated with HCl to give I [R1 = Cl, R2 = R3 = H].

IT 123318-82-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antiviral agent)

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DICTIONARY FILE UPDATES: 24 APR 2003 HIGHEST RN 505023-70-1

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Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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FILE COVERS 1907 - 25 Apr 2003 VOL 138 ISS 18
FILE LAST UPDATED: 24 Apr 2003 (20030424/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L3 SEL L2 1- CHEM : 3 TERMS
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L5 19 SEA FILE=HCAPLUS L4 AND (SYNTHES? OR PREP? OR MANUF?)
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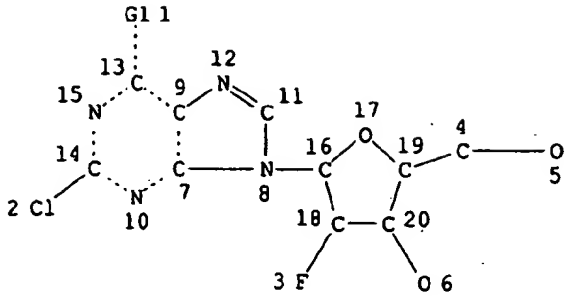

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L11 22 SEA FILE=REGISTRY SSS FUL L9
L12 20 SEA FILE=HCAPLUS L11/P
L13 7 SEA FILE=HCAPLUS L12 NOT L5

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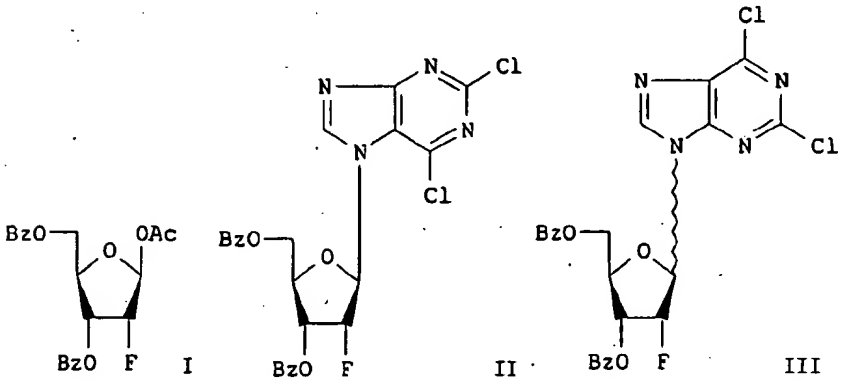
L13 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:674994 HCAPLUS
DOCUMENT NUMBER: 136:20198
TITLE: Synthesis and biological activity of 4'-C-hydroxymethyl-2'-fluoro-D-arabinofuranosylpurine nucleosides
AUTHOR(S): Shortnacy-Fowler, A. T.; Tiwari, K. N.; Montgomery, J. A.; Secrist, J. A., III
CORPORATE SOURCE: Southern Research Institute, Birmingham, AL, 35255-5305, USA
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2001), 20(4-7), 747-750
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 4'-C-hydroxymethyl-2'-fluoro-D-arabinofuranosylpurine nucleosides was prepd. and evaluated for cytotoxicity in human tumor cell lines. A convenient synthesis of the carbohydrate precursor 4-C-hydroxymethyl-3,5-di-O-benzoyl-2-fluoro-.alpha.-D-arabinofuranosyl bromide (13) was developed. Coupling of 13 with the sodium salt of 2,6-dichloropurine led to five target purine nucleosides.
IT **374782-67-9P 374782-68-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., antitumor activity, and cytotoxicity of 4'-C-hydroxymethyl-2'-fluoro-D-arabinofuranosylpurine nucleosides)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:10640 HCAPLUS
DOCUMENT NUMBER: 124:202895
TITLE: Convergent synthesis and cytostatic properties of 2-chloro-2'-deoxy-2'-fluoroadenosine and its N7-isomer
AUTHOR(S): Zaitseva, Galina V.; Sivets, Grigorii G.; Kazimierczuk, Zygmunt; Vilpo, Juhani A.; Mikhailopulo, Igor A.
CORPORATE SOURCE: Inst. Bioorg. Chem., Byelorussian Acad. Sci., Minsk, 220141, Belarus
SOURCE: Bioorganic & Medicinal Chemistry Letters (1995), 5(24), 2999-3002
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:202895
GI



AB Glycosylation of trimethylsilylated 2,6-dichloropurine with acetate I in anhyd. MeCN was investigated. In the presence of SnCl4, the reaction was regio- and stereoselective affording N7-.beta.-glycoside II (86%). The use of TMS-Tfl instead of SnCl4 afforded a .apprxeq.9:1 mixt. of the N9-.beta.- and -.alpha.-glycosides III (90%, combined). The title nucleosides were tested for their cytotoxicity.

IT 156357-18-5P, 2-Chloro-2'-deoxy-2'-fluoroadenosine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(convergent synthesis and cytostatic properties of chlorodeoxyfluoroadenosines)

IT 174462-89-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(convergent synthesis and cytostatic properties of chlorodeoxyfluoroadenosines)

L13 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:448387 HCAPLUS

DOCUMENT NUMBER: 122:255520
TITLE: Search for New Purine- and Ribose-Modified Adenosine Analogs as Selective Agonists and Antagonists at Adenosine Receptors
AUTHOR(S): Siddiqi, Suhaib M.; Jacobson, Kenneth A.; Esker, John L.; Olah, Mark E.; Ji, Xiao-duo; Melman, Neli; Tiwari, Kamal N.; Secrist, John A., III; Schneller, Stewart W.; et al.
CORPORATE SOURCE: Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 20892-0810, USA
SOURCE: Journal of Medicinal Chemistry (1995), 38(7), 1174-88
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The binding affinities at rat A1, A2a, and A3 adenosine receptors of a wide range of derivs. of adenosine have been detd. Sites of modification include the purine moiety (1-, 3-, and 7-deaza; halo, alkyne, and amino substitutions at the 2- and 8-positions; and N6-CH2-ring, -hydrazino, and -hydroxylamino) and the ribose moiety (2'-, 3'-, and 5'-deoxy; 2'- and 3'-O-methyl; 2'-deoxy 2'-fluoro; 6'-thio; 5'-uronamide; carbocyclic; 4'- and 3'-methyl; and inversion of configuration). (-)- And (+)-5'-noraristeromycin were 48- and 21-fold selective, resp., for A2a vs A1 receptors. 2-Chloro-6'-thioadenosine displayed a Ki value of 20 nM at A2a receptors (15-fold selective vs A1). 2-Chloroadenine-9-(.beta.-L-2'-deoxy-6'-lyxofuranoside) displayed a Ki value of 8 .mu.M at A1 receptors and appeared to be an antagonist, on the basis of the absence of a GTP-induced shift in binding vs a radiolabeled antagonist (8-cyclopentyl-1,3-dipropylxanthine). 2-Chloro-2'-deoxyadenosine and 2-chloroadenine-9-(.beta.-D-6'-thioarabinoside) were putative partial agonists at A1 receptors, with Ki values of 7.4 and 5.4 .mu.M, resp. The A2a selective agonist 2-(1-hexynyl)-5'-(N-ethylcarbamoyl)adenosine displayed a Ki value of 26 nM at A3 receptors. The 4'-Me substitution was poorly tolerated, yet when combined with other favorable modifications, potency was restored. Thus, N6-benzyl-4'-methyladenosine-5'-(N-methyluronamide) displayed a Ki value of 604 nM at A3 receptors and was 103- and 88-fold selective vs A1 and A2a receptors, resp. This compd. was a full agonist in the A3-mediated inhibition of adenylate cyclase in transfected CHO cells. The carbocyclic analog of N6-(3-iodobenzyl)adenosine-5'-(N-methyluronamide) was 2-fold selective for A3 vs A1 receptors and was nearly inactive at A2a receptors.

IT 156357-18-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(purine- and ribose-modified adenosine analogs as selective agonists and antagonists at adenosine receptors)

L13 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:483851 HCAPLUS
DOCUMENT NUMBER: 121:83851
TITLE: Synthesis and biologic activity of purine 2'-deoxy-2'-fluoro-ribonucleosides
AUTHOR(S): Thomas, H. Jeanette; Tiwari, Kamal N.; Clayton, Sarah Jo; Secrist, John A., III; Montgomery, John A.
CORPORATE SOURCE: South. Res. Inst., Birmingham, AL, 35255-5305, USA
SOURCE: Nucleosides & Nucleotides (1994), 13(1-3), 309-23

CODEN: NUNUD5; ISSN: 0732-8311
DOCUMENT TYPE: Journal
LANGUAGE: English
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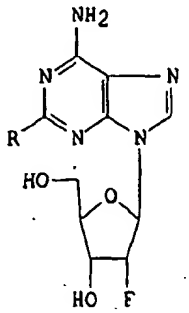

I

AB The synthesis of 3,5-di-O-benzoyl-2-deoxy-2-fluoro-D-ribofuranosyl bromide and its reaction with 2,6-dichloropurine by fusion and with mercuric cyanide catalysis is described. The resulting 2,6-dichloro-9-(3,5-di-O-benzoyl-2-deoxy-2-fluoro-.beta.-D-ribofuranosyl)purine was converted to 2'-deoxy-2'-fluoro-ribonucleosides, e.g. I (R = H, Cl, F). These nucleosides were cytotoxic to a no. of cell lines in culture. I (R = Cl, F) gave modest increases in lifespan when tested against the P388 leukemia in mice.

IT 156357-18-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antitumor activity of)

L13 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:459409 HCAPLUS
DOCUMENT NUMBER: 107:59409
TITLE: 2-Fluoro-arabinofuranosyl purine nucleosides as neoplasm inhibitors and parasiticides
INVENTOR(S): Watanabe, Kyoichi A.; Chu, Chung K.; Fox, Jack J.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 219829	A2	19870429	EP 1986-114412	19861017
EP 219829	A3	19880504		
EP 219829	B1	19921230		
R: DE, ES, FR, GB				
US 4751221	A	19880614	US 1985-789072	19851018
CA 1271192	A1	19900703	CA 1986-520646	19861016

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JP 62161797	A2	19870717	JP 1986-245654	19861017
JP 07023395	B4	19950315		
US 4918179	A	19900417	US 1988-189148	19880502
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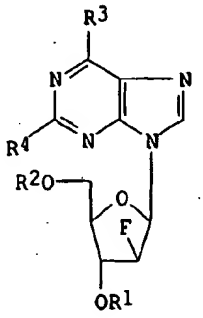

I

AB The title compds. (I; R1, R2 = H, acyl, aroyl; R3, R4 = H, halo, OR5, SR5,NR5R6, decylimino; R5, R6 = H, alkyl, aralkyl, acyl) were prepd. as neoplasm inhibitors and parasiticides. I (R1 = R2 = H, R3 = SH, R4 = NH2) was refluxed in H2O with Raney Ni to give I (R1 = R2 = R3 = H, R4 = NH2) (II). II had an ID50 of 2.0 .mu.M against mouse L 1210 leukemia cells.

IT **109303-89-1P 109303-90-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as parasiticide and neoplasm inhibitor)

L13 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:491327 HCAPLUS
DOCUMENT NUMBER: 105:91327
TITLE: Treatment of tumors in mammals
INVENTOR(S): Grindey, Gerald Burr; Hertel, Larry Wayne
PATENT ASSIGNEE(S): Lilly, Eli, and Co. , USA
SOURCE: Eur. Pat. Appl., 60 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 184365	A2	19860611	EP 1985-308547	19851125
EP 184365	A3	19880127		
EP 184365	B1	19930804		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8509008	A	19870729	ZA 1985-9008	19851125
CA 1264738	A1	19900123	CA 1985-496077	19851125
IL 77133	A1	19910131	IL 1985-77133	19851125
AT 92499	E	19930815	AT 1985-308547	19851125
DK 162965	B	19920106	DK 1985-5496	19851128
DK 162965	C	19920601		
AU 8550555	A1	19860612	AU 1985-50555	19851202

AU 581269	B2	19890216		
JP 61148193	A2	19860705	JP 1985-273161	19851203
JP 06037394	B4	19940518		
CN 85109409	A	19860827	CN 1985-109409	19851203
CN 1020194	B	19930331		
HU 39188	A2	19860828	HU 1985-4620	19851203
HU 194273	B	19880128		
ES 549547	A1	19870801	ES 1985-549547	19851203
US 5061793	A	19911029	US 1988-163571	19880303
US 5464826	A	19951107	US 1994-280687	19940726
PRIORITY APPLN. INFO.:			US 1984-677783	19841204
			US 1985-786419	19851010
			EP 1985-308547	19851125
			US 1988-163571	19880303
			US 1991-746441	19910816
			US 1993-99268	19930729

AB 2'-Deoxy-2',2'-difluoronucleosides are prepd. as cytostatic agents for neoplasm treatment. For example, 1-(4-amino-2-oxo-1H-pyrimidin-1-yl)-2-deoxy-2,2-difluororibose (I) (20.0 mg/kg i.p. on days 1, 5, and 9 after tumor implantation) gave 92-100% inhibition of 6C3HED lymphosarcoma, CA755 adenocarcinoma, P1534J lymphocytic leukemia, and X5563 myeloma in mice. I was prepd. by reaction of 3,5-bis(tert-butyldimethylsiloxy)-1-methanesulfonyloxy-2-deoxy-2,2-difluororibose with bis(trimethylsilyl)-N-acetylcytosine and deprotection. Tablets were prepd. contg. I 250, microcryst. cellulose 400, SiO2 10, and stearic acid 5 mg.

IT **103828-79-1P 103828-80-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as neoplasm inhibitor)

L13 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1970:44060 HCAPLUS
DOCUMENT NUMBER: 72:44060
TITLE: Nucleosides. LX. Fluorocarbohydrates. 22. Synthesis of 2-deoxy-2-fluoro-D-arabinose and 9-(2-deoxy-2-fluoro-.alpha. and .beta.-D-arabinofuranosyl)adenines
AUTHOR(S): Wright, John Arthur; Taylor, Norman F.; Fox, Jack J.
CORPORATE SOURCE: Sloan-Kettering Inst. for Cancer Res., New York, NY, USA
SOURCE: Journal of Organic Chemistry (1969), 34(9), 2632-35
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nucleophilic attack of KHF2 on Me 2,3-anhydro-5-O-benzyl-.alpha.-D-riboside occurred largely at the 2 position (in contrast to the .beta.-D anomer) and leads to Me 5-O-benzyl-2-deoxy-2-fluoro-.alpha.-D-arabinoside (I), thu s achieving the first direct synthesis of a 2-fluoropentose derivative. From I, 2-deoxy-2-fluoro-D-arabinose is obtained. Fusion of 1,3-di-O-acetyl-5-O-benzyl-2-deoxy-2-fluoro-D-arabinose with 2,6-dichloropurine affords a readily resolved .alpha.-.beta. mixt. of 9-glycosyl-purine nucleosides, which are converted into 9-(2-deoxy-2-fluoro-.alpha.-and .beta.-D-arabinofuranosyl)adenines. Confirmation of the anomeric configuration of these nucleosides is obtained by conversion into their 5'-toluenesulfonates and by cyclization of the .beta. anomer to its 3,5'-cyclonucleoside.

IT **20187-81-9P 20227-40-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

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E1 THROUGH E10 ASSIGNED

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DICTIONARY FILE UPDATES:  24 APR 2003  HIGHEST RN 505023-70-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

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Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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               20227-40-1/BI OR 374782-67-9/BI OR 374782-68-0/BI)

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L14  ANSWER 1 OF 10  REGISTRY  COPYRIGHT 2003 ACS
RN   374782-68-0  REGISTRY
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Searched by M. Smith

CN 9H-Purin-6-amine, 2-chloro-9-[2-deoxy-2-fluoro-4-C-(hydroxymethyl)-.beta.-D-threo-pentofuranosyl]- (9CI) (CA INDEX NAME)
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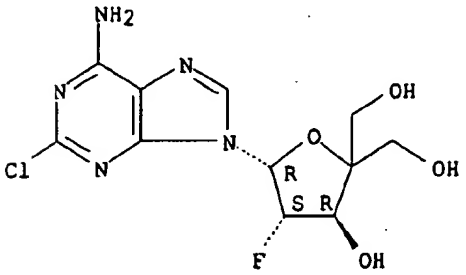
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

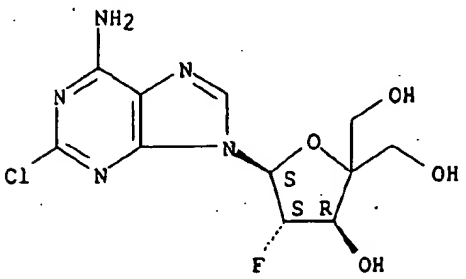
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:20198

REFERENCE 2: 136:6249

L14 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 374782-67-9 REGISTRY
CN 9H-Purin-6-amine, 2-chloro-9-[2-deoxy-2-fluoro-4-C-(hydroxymethyl)-.alpha.-D-threo-pentofuranosyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C11 H13 Cl F N5 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

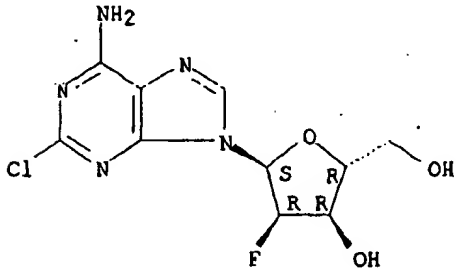
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 136:20198

REFERENCE 2: 136:6249

L14 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 174462-89-6 REGISTRY
CN 9H-Purin-6-amine, 2-chloro-9-(2-deoxy-2-fluoro-.alpha.-D-ribofuranosyl)-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H11 Cl F N5 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

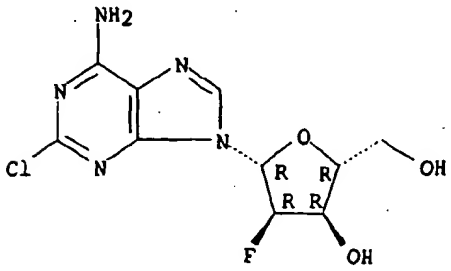
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 124:202895

L14 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 156357-18-5 REGISTRY
CN Adenosine, 2-chloro-2'-deoxy-2'-fluoro- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Chloro-2'-deoxy-2'-fluoroadenosine
FS STEREOSEARCH
MF C10 H11 Cl F N5 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

Absolute stereochemistry.

Searched by M. Smith



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:346991

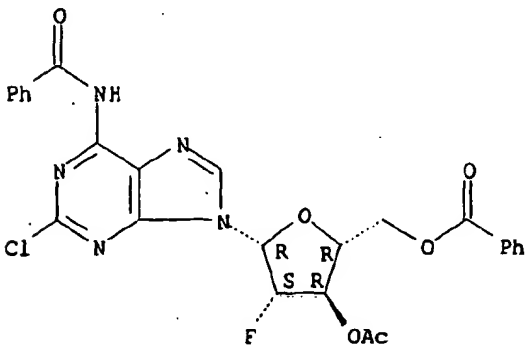
REFERENCE 2: 124:202895

REFERENCE 3: 122:255520

REFERENCE 4: 121:83851

L14 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 109303-90-4 REGISTRY
CN Benzamide, N-[9-(3-O-acetyl-5-O-benzoyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-2-chloro-9H-purin-6-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H21 Cl F N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)

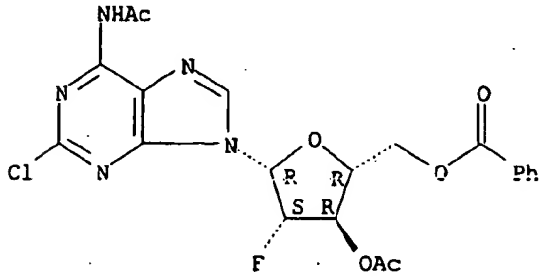
Searched by M. Smith

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 107:59409

L14 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN **109303-89-1** REGISTRY
CN Acetamide, N-[9-(3-O-acetyl-5-O-benzoyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-2-chloro-9H-purin-6-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H19 Cl F N5 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



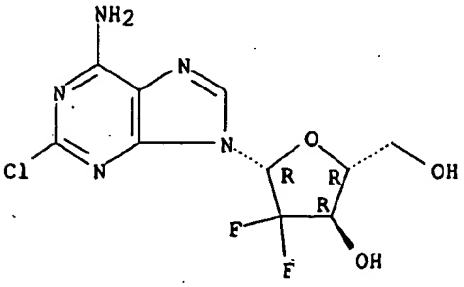
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 107:59409

L14 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN **103828-80-4** REGISTRY
CN Adenosine, 2-chloro-2'-deoxy-2',2'-difluoro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H10 Cl F2 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



Searched by M. Smith

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

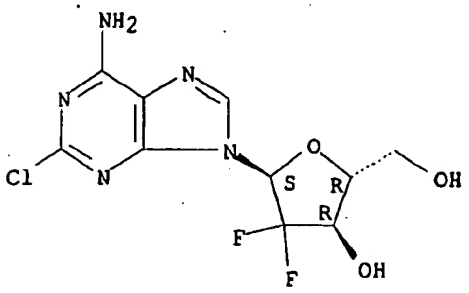
REFERENCE 1: 131:223117

REFERENCE 2: 130:346991

REFERENCE 3: 105:91327

L14 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 103828-79-1 REGISTRY
CN 9H-Purin-6-amine, 2-chloro-9-(2-deoxy-2,2-difluoro-.alpha.-D-erythro-pentofuranosyl)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C10 H10 Cl F2 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



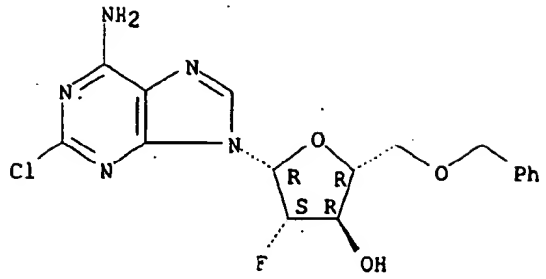
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 105:91327

L14 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 20227-40-1 REGISTRY
CN Adenine, 9-(5-O-benzyl-2-deoxy-2-fluoro-.beta.-D-arabinofuranosyl)-2-chloro- (8CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H17 Cl F N5 O3
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



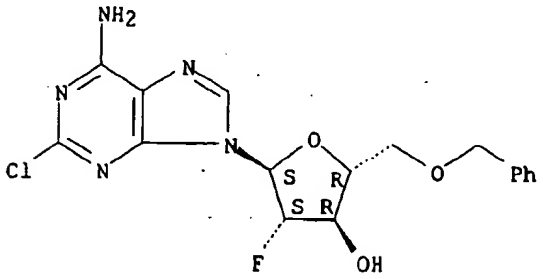
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 72:44060

L14 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2003 ACS
RN 20187-81-9 REGISTRY
CN Adenine, 9-(5-O-benzyl-2-deoxy-2-fluoro-.alpha.-D-arabinofuranosyl)-2-chloro- (8CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H17 Cl F N5 O3
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 72:44060

=> d stat que l26 nos
L2 1 SEA FILE=REGISTRY "9H-PURIN-6-AMINE, 2-CHLORO-9-(2-DEOXY-2-FLUORO-.BETA.-D-ARABINOFURANOSYL)-"/CN
L3 SEL L2 1- CHEM : 3 TERMS
L4 43 SEA FILE=HCAPLUS L3

Searched by M. Smith

```
L5          19 SEA FILE=HCAPLUS L4 AND (SYNTHES? OR PREP? OR MANUF?)
L9             STR
L11         22 SEA FILE=REGISTRY SSS FUL L9
L12         20 SEA FILE=HCAPLUS L11/P
L13          7 SEA FILE=HCAPLUS L12 NOT L5
L16       1804 SEA FILE=REGISTRY 2(W)CHLORO?(W)6(W)(ALKOXY? OR METHOXY? OR
               ETHOXY?)
L17       9543 SEA FILE=REGISTRY ARABINOFURANOSYL?
L18     113365 SEA FILE=REGISTRY PURIN?
L19      13471 SEA FILE=REGISTRY ADENINE?
L21       1420 SEA FILE=HCAPLUS 2(W)CHLORO?(W)6(W)(ALKOXY? OR METHOXY? OR
               ETHOXY?) OR L16
L22      13889 SEA FILE=HCAPLUS L17 OR ARABINOFURANOSYL?
L23     301642 SEA FILE=HCAPLUS L18 OR L19 OR PURIN? OR ADENIN?
L24       3316 SEA FILE=HCAPLUS L22(L)L23
L25          1 SEA FILE=HCAPLUS L24 AND L21
L26          1 SEA FILE=HCAPLUS L25 NOT (L5 OR L13)

=> d ibib abs hitstr

L26 ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        1991:445941  HCAPLUS
DOCUMENT NUMBER:         115:45941
TITLE:                   6-Methoxypurine arabinoside as a selective and potent
                         inhibitor of varicella-zoster virus
AUTHOR(S):               Averett, Devron R.; Koszalka, George W.; Fyfe, James
                         A.; Roberts, Grace B.; Purifoy, Dorothy J. M.;
                         Krenitsky, Thomas A.
CORPORATE SOURCE:        Wellcome Res. Lab., Research Triangle Park, NC, 27709,
                         USA
SOURCE:                  Antimicrobial Agents and Chemotherapy (1991), 35(5),
                         851-7
                         CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB  Seven 6-alkoxypurine arabinosides were synthesized and evaluated for in
    vitro activity against varicella-zoster virus (VZV). The simplest of the
    series, 6-methoxypurine arabinoside (ara-M), was the most potent, with 50%
    inhibitory concns. ranging from 0.5 to 3 .mu.M against eight strains of
    VZV. This activity was selective. The ability of ara-M to inhibit the
    growth of a variety of human cell lines was at least 30-fold less (50%
    effective concn., >100 .mu.M) than its ability to inhibit the virus.
    Enzyme studies suggested the mol. basis for these results. Of the seven
    6-alkoxypurine arabinosides, ara-M was the most efficient substrate for
    VZV-encoded thymidine kinase as well as the most potent antiviral agent.
    In contrast, it was not detectably phosphorylated by any of the 3 major
    mammalian nucleoside kinases. Upon direct comparison, ara-M was
    appreciably more potent against VZV than either acyclovir or adenine
    arabinoside (ara-A). However, in the presence of an adenosine deaminase
    inhibitor, the arabinosides of adenine and 6-methoxypurine were equipotent
    but not equally selective; the adenine congener had a much less favorable
    in vitro chemotherapeutic index. Again, this result correlated with data
    from enzyme studies in that ara-A, unlike ara-M, was a substrate for 2
    mammalian nucleoside kinases. Unlike acyclovir and ara-A, ara-M had no
    appreciable activity against other viruses of the herpes group. The
    potency and selectivity of ara-M as an anti-VZV agent in vitro justify its
    further study.
IT  91969-06-1P 121032-23-3P 121032-29-9P
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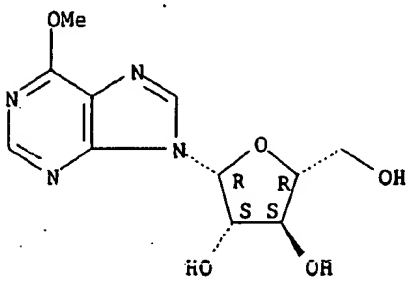
Searched by M. Smith

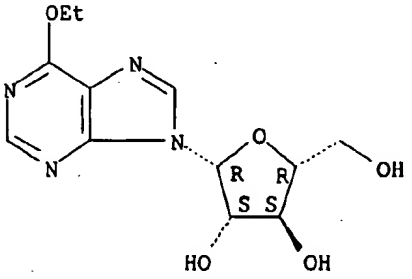
121032-30-2P 134978-72-6P 134978-73-7P
134978-74-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antiviral activity of, structure in relation to)
RN 91969-06-1 HCAPLUS
CN 9H-Purine, 9-.beta.-D-arabinofuranosyl-6-methoxy- (7CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



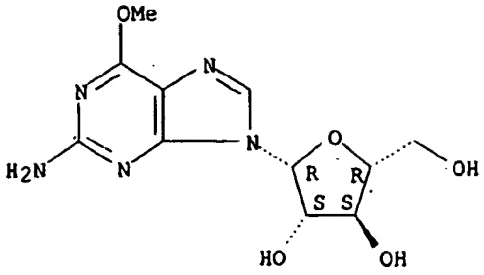
RN 121032-23-3 HCAPLUS
CN 9H-Purine, 9-.beta.-D-arabinofuranosyl-6-ethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



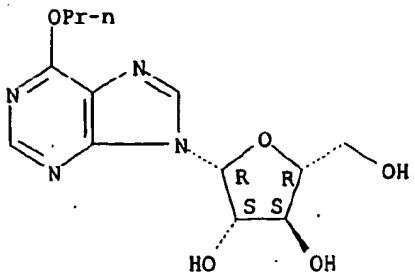
RN 121032-29-9 HCAPLUS
CN 9H-Purin-2-amine, 9-.beta.-D-arabinofuranosyl-6-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



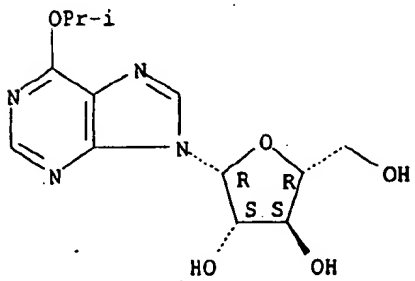
RN 121032-30-2 HCAPLUS
CN 9H-Purine, 9-.beta.-D-arabinofuranosyl-6-propoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



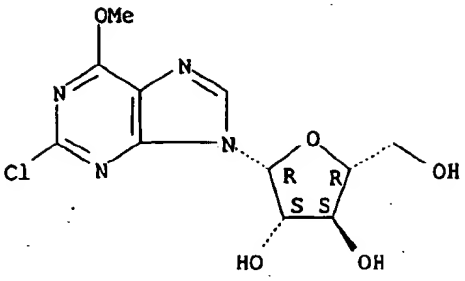
RN 134978-72-6 HCAPLUS
CN 9H-Purine, 9-.beta.-D-arabinofuranosyl-6-(1-methylethoxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 134978-73-7 HCAPLUS
CN 9H-Purine, 9-.beta.-D-arabinofuranosyl-2-chloro-6-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 134978-74-8 HCAPLUS
CN 9H-Purin-2-amine, 9-.beta.-D-arabinofuranosyl-6-ethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.